Final Office Action on the Merits of a RCE

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 17, 2011 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Application

3. Claims 39-76 are pending in the present application. The instant claims stand rejected as indicated below.

Claim Rejections - 35 USC § 112

4. The rejection of claims 57-64 under 35 USC 112, first paragraph, as failing to comply with the written description requirement is maintained.

Applicant argues the claimed invention is clearly defined in the original specification and reference is made to the definition of "recurrence of cancer " by the

American Society of Clinical Oncology. Applicant's argument was considered but not persuasive for the following reasons.

First, 35 USC 112 requires the specification contain a written description of the invention in "such full, clear, concise and exact terms" as to enable the skilled artisan to use the same.

Secondly, the issue is not the definition of the phrase *recurrence of cancer*. As noted by applicant and would have been obvious to the skilled artisan in the art at the time of the present invention, the above-mentioned phrase refers to the cancer coming back after treatment. The issue here is whether the present specification clearly defines the claimed invention, i.e., "reducing the likelihood of a recurrence of estrogen-sensitive breast cancer in a patient" after treatment with the claimed compounds. However, the first step in said treatment method is the ability of the skilled artisan in the art to be able to identify patients in need of treatment in order to reduce the likelihood of a recurrence of said estrogen-sensitive breast cancer. The present specification lacks description of how said determination is made as well as any example showing the reduction of the "likelihood" of said breast cancer. Therefore, the skilled artisan in the art at the time of the present invention would have been unable to use the claimed invention as encompassed by the instant claims.

For these reasons and those given in the previous Office Actions, the rejection of claims 57-64 under 35 USC 112, first paragraph, as failing to comply with the written description requirement is maintained.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 76 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claim is indefinite for the following reasons:

(a) Defining a disease(s) by its (their) underlying cause, i.e., SERM-responsive disease state, renders the scope of the intended uses indeterminate since the claim language may read on diseases not yet known to be affected by such action or in ways not yet understood. Additionally, determining whether a given disease responds or not to such a mode of action involves much experimentation since a negative response from one patient does not mean the drug is not useful as no drug has 100% effectiveness. Thus, what "success rate" determines if a particular compound is effective and how many patients (and dosage regimens) need to be tested. The test for determining compliance with 35 USC 112, second paragraph, is whether Applicant has clearly defined "their" invention not what may be discovered by future research as this type of claim language clearly requires;

(b) The instant claim recites "a SERM-responsive disease state as described in the specification". However, MPEP 2173.05(s) states, "Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than

duplicating a drawing or table into the claim". This condition is not met here, since it is practical to define the invention by incorporating the disease state(s) into the claim. *Ex parte Fressola*, 27 USPQ 2d 1609 (BPAI 1993); and

(c) claim 76 recites "a compounds as set forth in claim 39". However, claim 39 is drawn to a method of treating not compounds as recited by the instant claim.

For these reasons, the skilled artisan in the art would be unable to determine the metes and bound of the claimed invention.

Claim Rejections - 35 USC § 103

7. The rejection of claims 39-75 under 35 USC 103(a) over van den Broek et al. (US 3,972,906) is maintained and claim 76 is rejected under 35 USC 103(a) over van den Broek et al. (US 3,972,906).

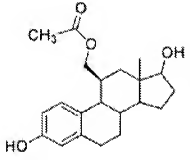
Applicant argues that all of the claimed methods rely on SERM activity which is not taught by van den Broek. Applicant also argues the reference (a) does not exemplify the biological activity of the claimed compounds, (b) discloses estrogenic activity of short-chain groups at the 11β-position which is corroborated by experiments presented on pages 22-23 of the present application and (c) teaches away from the present invention because estrogen agonists are contraindicated in patients with or at risk for estrogen-sensitive cancers. Applicant's argument was considered but not persuasive for the following reasons.

First, a reference is not limited to its working examples. It must be evaluated for what it teaches those of ordinary skill in the art. *In re Boe*, 355 F.2d 961, 148 USPQ 507 (CCPA 1966). *In re Chapman*, 357 F.2d 418, 148 USPQ 711 (CCPA 1966).

As noted by MPEP § 2123 (II), nonpreferred and alternative embodiments constitute prior art. "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments." *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). The examiner agrees the reference exemplifies 11β-methoxymethyl-ethinyl estradiol and 11β-chloromethyl-ethinyl estradiol, i.e., short-chain groups at the 11β-position. However, van den Broek teaches 11βalkoxy methyl as well as 11β-alkcarbonyloxymethyl and, thus, is not limited to the exemplified compounds.

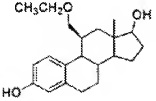
Secondly, applicant refers to data on pages 22-25 of the present specification and argues the activity of the compounds. However, the issue is not the activity of the compounds as disclosed by the present specification but the teaching by the prior art of the use of said compounds in treating estrogen-deficiency syndromes which is inclusive of menopausal symptoms and breast cancer as is well known in the art. The fact that the art at the time of the present invention did not realize the compounds were SERM does not nullify the teaching of the prior art or results in a teaching away as suggested by applicant. Discovery of a new activity of a prior art compound does not lend patentability to the utilization of said compound(s) in the method as taught or made obvious by the prior art.

In addition, none of the compounds found in Tables 1 and 2 of the present specification is encompassed by the van den Broek as evidenced by the structures thereof. See for example,

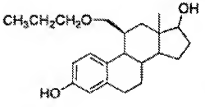


E11-1,2Rev
agonist

(Table 1, page 23 of the present application);

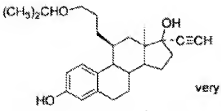


E11-1,2ether
agonist

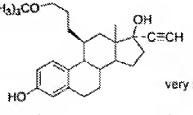


E11-1,3 ether
strong antagonist

and



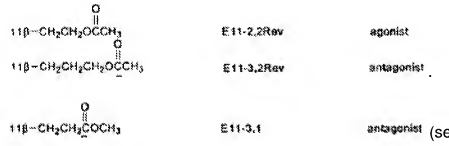
17α-Ethynyl
E11-3,iPr ether
very strong antagonist



17α-Ethynyl
E11-3,tBu ether
very strong antagonist

(Table 2, page 24 of the present application). Therefore, there is no evidence on record to support applicant's argument of unexpected and/or unobviousness of the

claimed invention over the cited reference. Also, as shown in Tables 1 and 2 any change may reverse the activity of the compound, for example,



(see discussion on page 23 of the present specification).

> Additionally, as recognized by MPEP §716.02(d),
>
> Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of non-obviousness **must be commensurate in scope with the claims** which the evidence is offered to support." In other words, the showing of unexpected results must be reviewed to see if the results occur over the entire claimed range. *In re Clemens*, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980).

The data shown in the present specification does not commensurate in scope with the claimed compounds.

Lastly, evidence of unexpected results must be weighed against supporting prima facie obviousness in making a final determination of the obviousness of the claimed invention. *In re May*, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978). The issue here is not the identification of the compounds as SERMs but the obviousness of utilizing said compounds as taught by the prior art. The fact that applicant recognized an advantage which flows from the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). As recognized by MPEP §2121, prior art is presumed to be enabling; "proof of efficacy is not required for a prior art reference to be

enabling for purposes of anticipation." *Impax Labs. Inc. v. Aventis Pharm. Inc.*, 468 F.3d 1366, 1383, 81 USPQ2d 1001, 1013 (Fed. Cir. 2006).

In summary, van den Broek teaches a genus of compounds useful in treating estrogen-deficiency syndromes. The art teaches both menopausal symptoms and breast cancer as estrogen-deficiency syndromes and, thus, the use of van den Broek compounds in treating said conditions would have been obvious at the time of the present invention.

For these reasons and those given in the previous Office Actions, the rejection of claims 39-75 under 35 USC 103(a) over van den Broek et al. (US 3,972,906) is maintained and claim 76 is rejected under 35 USC 103(a) over van den Broek et al. (US 3,972,906).

8. The rejection of claims 39-75 under 35 USC 103(a) over van den Broek et al. (US 3,972,906) in view of Cameron et al. (US 2001/0025051), Palkowitz (US 6,268,361) and Bodor et al. (US 4,617,298) is maintained and claim 76 is rejected under 35 USC 103(a) over van den Broek et al. (US 3,972,906) in view of Cameron et al. (US 2001/0025051), Palkowitz (US 6,268,361) and Bodor et al. (US 4,617,298).

Applicant's argument in regards to van den Broek is as discussed above in #7.

Applicant argues (a) the compound of Cameron are structurally different from the claimed compounds and are contraindicated for use in treatment of estrogen-sensitive cancers, (b) Palkowitz, like Cameron, teaches estrogen agonists are to be avoided in treating estrogen-sensitive cancers and (c) Bodor teaches structurally different

compounds and only make an oblique reference to the use of estrogen compounds in the treatment of breast cancer. Said use has been discontinued because of the tendency to exacerbate or worsen estrogen-sensitive cancer. Applicant's argument was considered but not persuasive for the following reasons.

The examiner agrees that the compounds of Cameron, Palkowitz and Bodor are structurally different from those of the claimed compounds. However, as noted in previous Office Actions, these references were utilized for their teaching of estrogens in the treatment of menopausal symptoms and breast cancer.

Applicant argues Cameron and Palkowitz teach the use of estrogen is contraindicated in the treatment of estrogen-sensitive cancers. However, as noted by applicant, the use of estrogen in treating breast cancer and menopausal symptoms was known in the art as evidenced by Bodor, Cameron and Palkowitz. The issue is not whether said use is contraindicated but whether said use was made obvious by the cited references.

The fact remains that the compounds of van den Broek are encompassed by the instant claims. The reference also teaches the use of said compounds in treating estrogen-deficiency syndromes which as evidenced by the art is inclusive of menopausal symptoms and breast cancer. Therefore, the use of the compounds of van den Broek in treating said conditions would have be prima facie obvious at the time of the present invention.

As noted above in #7, the data shown in the present specification does not include the prior art compounds and, thus, does not provide support for applicant's argument of unexpected results.

For these reasons and those given in the previous Office Actions, the rejection of claims 39-75 under 35 USC 103(a) over van den Broek et al. (US 3,972,906) in view of Cameron et al. (US 2001/0025051), Palkowitz (US 6,268,361) and Bodor et al. (US 4,617,298) is maintained and claim 76 is rejected under 35 USC 103(a) over van den Broek et al. (US 3,972,906) in view of Cameron et al. (US 2001/0025051), Palkowitz (US 6,268,361) and Bodor et al. (US 4,617,298).

Telephone Inquiry

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BARBARA P. BADIO whose telephone number is (571)272-0609. The examiner can normally be reached on M-F from 6:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/BARBARA P. BADIO/
Primary Examiner, Art Unit 1628